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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/551,380	04/18/2000	Donald Choy Chang	MLY-5	2514

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EXAMINER

FRONDA, CHRISTIAN L

ART UNIT PAPER NUMBER

1652

DATE MAILED: 07/30/2002 15

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.
09/551,380

Applicant(s)
Chang et al.

Examiner
Christian L. Fronda

Art Unit
1652



-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☐ Responsive to communication(s) filed on _____.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-7, 25, 26, and 28-39 is/are pending in the application.
- 4a) Of the above, claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-7, 25, 26, and 28-39 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claims _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.
If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

- 13) ☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
a) ☐ All b) ☐ Some* c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
*See the attached detailed Office action for a list of the certified copies not received.
- 14) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).
a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

- 1) ☐ Notice of References Cited (PTO-892) 4) ☐ Interview Summary (PTO-413) Paper No(s). _____
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948) 5) ☐ Notice of Informal Patent Application (PTO-152)
- 3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s). _____ 6) ☐ Other:

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DETAILED ACTION

1. In the AMENDMENT A dated 5/3/2002 (Paper No. 13), Applicants have canceled claims 8-24 and 27, amended claims 1, 4, 5, 6, and 7, and added new claims 28-39.
2. Claims 1-7, 25, 26, and 28-39 are under consideration in this Office Action.

Claim Objections

3. Claims 35, 36, 38, and 39 are objected to because of the following informalities: the claims 35 and 36 recite non-elected subject matter, specifically, SEQ ID NOs: 7-13, 36-40, 42-51, and 55. Applicant is required to cancel the claims or amend the claims to recite the elected subject matter which is D9 (SEQ ID NO: 41) and SEQ ID NO: 4.

Claim Rejections - 35 U.S.C. § 101

4. 35 U.S.C. 101 reads as follows:
Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.
5. Claims 1-7, 25, 26, and 28-39 are rejected under 35 U.S.C. 101 because the claims are directed toward non-statutory subject matter. In the absences of the hand of man, naturally occurring proteins and peptides are considered non-statutory subject mater. See Diamond v. Chakrabarty, 206 USPQ 193 (1980). This rejection may be overcome by amending the claims to contain the phrase "an isolated and purified peptide".

Claim Rejections - 35 U.S.C. § 112, 1st Paragraph

6. The following is a quotation of the first paragraph of 35 U.S.C. 112:
The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to

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make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

7. Claims 1-7, 25, 26, and 28-39 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

This is a new matter rejection. Regarding the fluorescent protein, the recitation of the phrase “comprising an 11-stranded β -barrel formed from 11 β -sheets surrounding a chromophore-containing co-axial α -helix, each of said β -sheets forming said β -barrel joined by a loop structure to at least one other adjacent β -sheet forming said β -barrel” has no support in the specification or claims as originally filed. The specification, however, only discloses a fluorescent protein consisting of the amino acid sequence of SEQ ID NO: 41.

8. Claims 1-7, 25, 26, and 28-39 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a green fluorescent protein (GFP) having a protease cleavage site and an amino acid sequence consisting of SEQ ID NO: 41; does not reasonably provide enablement for any fluorescent protein “comprising an 11-stranded β -barrel formed from 11 β -sheets surrounding a chromophore-containing co-axial α -helix, each of said β -sheets forming said β -barrel joined by a loop structure to at least one other adjacent β -sheet forming said β -barrel”. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

The claimed invention requires the crystal structure of any fluorescent protein in order to identify, determine the number, and position of any β -sheet structure. While molecular biological techniques and several crystallization methods for proteins are known in the prior art and the skill of the artisan are well developed, knowledge regarding the specific fluorescent protein and how to obtain a suitable crystal for structure determination by X-ray is lacking. Thus, searching for any fluorescent protein and for crystallization conditions to obtain an adequate crystal of any fluorescent protein for structure determination by x-ray diffraction method is well outside the realm of routine experimentation and predictability in the art of success is extremely low, see Branden et al. page 271 cited in the previous Office Action dated 10/24/2001 (Paper No. 10).

The conditions of crystallization is highly dependent on the fluorescent protein itself and any minor change in the amino acid sequence may require search for new crystallization conditions. The amount of experimentation to identify the specific fluorescent protein and conditions to grow a single crystal suitable for structure determination in order to identify, determine the number, and position of any β -sheet structure is enormous. Since routine experimentation in the art does not include screening for vast numbers of fluorescent proteins and

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crystallization conditions where the expectation of obtaining the desired crystal is unpredictable, the Examiner finds that one skilled in the art would require additional guidance, such as information regarding the exact fluorescent protein to be crystallized and the conditions under which the fluorescent protein would crystallize and produce an adequate crystal for structural determination by X-ray. Without such a guidance, the experimentation left to those skilled in the art is undue.

Claim Rejections - 35 U.S.C. § 102

9. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless --

(a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

10. Claims 1, 2, 25, 26, 28, 29, and 34 are rejected under 35 U.S.C. 102(b) as being anticipated by Xu et al. This reference was attached to the previous Office Action dated 10/24/2001 (Paper No. 10).

Xu et al. teach a green fluorescent protein (GFP) that is linked by an 18 amino acid peptide containing the caspase-3 (CPP32) cleavage site, DEVD, to blue fluorescent protein (BFP), wherein cleavage at the cleavage site results in alteration of at least one of the emission and excitation spectra (see entire publication and Figure 2). The GFP taught by Xu et al. is expected to be an 11-stranded β -barrel with a coaxial α -helix, with the chromophore forming from the central helix as indicated by the Ormo et al. reference stated in the specification on page 10, 1st paragraph. Thus, the reference teachings anticipate the claimed invention.

Conclusion

11. No claim is allowed.

12. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire **THREE**

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MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

13. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Christian L. Fronda whose telephone number is (703)305-1252. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ponnathapura Achutamurthy, can be reached at (703)308-3804. The fax phone number for this Group is (703)308-0294. Any inquiry of a general nature or relating to the status of this application should be directed to the Group 1600 receptionist whose telephone number is (703)308-0196.

CLF



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